THE
AMERICAN NATURALIST

VOL. XLVIII *September, 1914* NO. 573

STUDIES ON INBREEDING. V

INBREEDING AND RELATIONSHIP COEFFICIENTS[1]

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IN the discussion of inbreeding coefficients contained in a series of recent papers from this laboratory[2] no mention has been made of an important consideration which arises in connection with such coefficients. The further problem, to which we may now turn, may be stated in the following way.

The pedigree of an individual consists of two halves. One of these halves is made up of the sire and his ancestors; the other of the dam and her ancestors. Following the conception of inbreeding set forth in detail in the earlier papers of this series it is plain that the values of the coefficients of inbreeding for a particular pedigree are composed of the following elements.

1. The occurrence of the same individual animals more than once on the sire's side of the pedigree only.

2. The occurrence of the same individual animals more than once on the dam's side of the pedigree only.

[1] Papers from the Biological Laboratory of the Maine Agricultural Experiment Station, No. 69.

[2] Pearl, R., "Studies on Inbreeding. I. A Contribution Towards an Analysis of the Problem of Inbreeding," AMER. NAT., Vol. XLVII, pp. 577–614, 1913; "The Measurement of the Intensity of Inbreeding," *Me. Agr. Expt. Sta. Bul.*, 215, pp. 123–138, 1913. Pearl, R., and Miner, J. R., "Studies on Inbreeding. III. Tables for Calculating Coefficients of Inbreeding," Me. Agr. Expt. Sta. Ann. Rept. for 1913, pp. 191–202, 1913.

3. The reappearance of animals which appear first on one side of the pedigree (either the sire's or the dam's) on the other side.

If only 1 and 2 are to be found in the pedigree it means that the sire and the dam are totally unrelated (within the limits covered by the pedigree in the particular case). On the other hand, the occurrence of 3 means that sire and dam are in some degree related, and that a portion of the observed inbreeding arises because of that fact. Now the coefficients of inbreeding, in and of themselves, tell nothing about what proportionate part has been played by these three elements in reaching the final result. It is a matter of great importance to have information on this point, because of its genetic significance. It is the purpose of this paper to describe a general method for obtaining this desired information.

The first step in the method, stated briefly, is to break up the pedigree elimination table formed to get the successive values of $p_{n+1} - q_{n+1}$, in our former notation, into four different parts. One of these parts will include the primary reappearance on the sire's side of the pedigree of such animals as appear first on the same side. This may be called the "male only" table. The second part will include the primary reappearance on the dam's side of such animals as first appear on the same side. This is the "female only" table. The third part will include the primary reappearance on the dam's side of such animals as first appear on the sire's side. The fourth part is the reverse of the third. These last two may be called the "cross tables." The sums of the totals of these partial tables will give the total $p_{n+1} - q_{n+1}$ values for the successive generations.

The formation of the tables on this plan may be illustrated with some examples. These examples will also show the skeleton method of writing pedigree elimination tables, which saves much labor. This was referred to, but not significantly illustrated, in the earlier papers. It consists simply in doubling the total of the column for each generation rather than the separate items.

TABLE I

PARTIAL PEDIGREE ELIMINATION TABLE FOR KING MELIA RIOTER 14TH SHOWING THE PRIMARY REAPPEARANCES ON THE SIRE'S SIDE OF THE PEDIGREE OF ANIMALS WHICH FIRST APPEAR ON THAT SIDE

Generation	2	3	4	5	6	7	8	9	10	11	12
Melia Ann's Son			1	(2)[3]							
Melia Ann 3d				1	(6)[3]						
Lucy's Stoke Pogis					3						
Melia Ann					2						
St. Lambert Boy					1						
Letty Rioter					1						
Allie of St. Lambert					1						
Lord Aylmer					1						
Amelia 2d					1	(32)[3]					
Victor Hugo						1					
Oakland's Nora						1					
Stoke Pogis 3d						1					
Bachelor of St. Lambert						1					
Sir George of St. Lambert						1					
Diana's Rioter						1					
Orloff						1					
Lorne						1					
Hugo's Victoria						1	(82)[3]				
Victor Hugo							1				
Pauline							1				
Canada's John Bull							1				
Oakland's Nora							1				
Stoke Pogis 3d							7				
Kathleen of St. Lambert							1				
Lord Lisgar							4				
Lucy of St. Lambert							2				
Diana of St. Lambert							1				
Pet of St. Lambert							1				
Orloff							1				
Bachelor of St. Lambert							1				
Ida of St. Lambert							1	(210)[3]			
Victor Hugo								2			
Stoke Pogis 3d								2			
Lord Lisgar								3			
Lorne								1			
Amelia								1	(438)[3]		
Lord Lisgar									1		
Pride of Windsor									2		
Laval									1		
Amelia									2		
Victor Hugo									3	(894)[3]	
Laval										1	
Amelia										1	
Lisette										1	
Berthe										1	
Totals			1	3	16	41	105	219	447	898	1,796

[3] In this and the following table the numbers in brackets are in each case twice the sum of the numbers in the preceding column. They represent the accumulated ancestral reduplication up to the generation in question.

The pedigree for 12 ancestral generations of the Jersey bull King Melia Rioter 14th (103901) may be taken as the first illustration.

TABLE II

PARTIAL PEDIGREE ELIMINATION TABLE FOR KING MELIA RIOTER 14TH SHOWING THE PRIMARY REAPPEARANCES ON THE DAM'S SIDE OF THE PEDIGREE OF ANIMALS WHICH FIRST APPEAR ON THAT SIDE

Generation	2	3	4	5	6	7	8	9	10	11	12
King's Rioter Lad	—	—	—	1	2	4	8	16	32	64	128

Table III is clearly the one which demands special attention. As will shortly appear, it is the most important for the theory of inbreeding. Let us attempt its analysis. Just what does the first entry mean genetically? It states that King Melia Rioter, an animal which first appeared on the sire's side of the pedigree, reappeared in the second ancestral generation on the dam's side. What this clearly means is that at least one half of all the dam's ancestors, in the third and higher ancestral generations, *are identically the same animals as are ancestors of the*

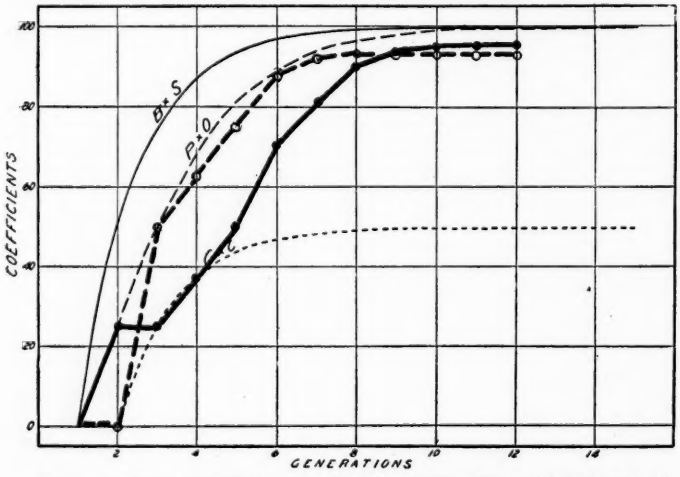

FIG. 1. Diagram showing (*a*) the total inbreeding (heavy solid line) and (*b*) the relationship (heavy broken line) curves for the Jersey bull, King Melia Rioter 14th. The high order of the inbreeding and relationship between the sire and dam in this case is evident by comparison with the lighter lines, which give the maximum values for continued brother × sister, parent × offspring and cousin × cousin breeding.

sire. The next entry in Table III indicates that in the fourth and higher ancestral generations at least 5/8 of all the dam's ancestors were the same individual animals as were also ancestors of the sire. One half of them were the same before the reappearance of St. Lambert's Rioter King. He makes up the additional 1/8 of the dam's ancestry.

TABLE III

PARTIAL PEDIGREE ELIMINATION TABLE FOR KING MELIA RIOTER 14TH SHOWING THE PRIMARY REAPPEARANCES ON THE DAM'S SIDE OF THE PEDIGREE OF ANIMALS WHICH FIRST APPEAR ON THE SIRE'S SIDE

Generation	2	3	4	5	6	7	8	9	10	11	12
King Melia Rioter	1	(2)	(4)								
St. Lambert's Rioter King			1	(10)							
King of St. Lambert				1							
St. Lambert Boy				1	(24)						
St. Lambert Boy					2						
Oakland's Nora					1						
St. Lambert's Rioter King					1	(56)					
St. Lambert Boy						1					
King of St. Lambert						1					
St. Lambert's Letty						1	(118)				
Letty Coles 2d							1	(238)			
King of St. Lambert								1			
Louise's Grace								1			
Totals	1	2	5	12	28	59	119	240	480	960	1,920

From these tables it is obvious that a very considerable portion of the inbreeding shown in the pedigree of King Melia Rioter 14th arises from the fact that his sire and dam were closely related. Furthermore, both sire and dam are closely inbred in their own lines. The curve of total inbreeding in this case is shown in Fig. 1, along with the curves for continued brother × sister, parent by offspring, and cousin × cousin mating.

TABLE IV

SUMMARIZED PEDIGREE ELIMINATION TABLE FOR KING MELIA RIOTER 14TH

Generation	2	3	4	5	6	7	8	9	10	11	12
♂ only			1	3	16	41	105	219	447	898	1,796
♀ only				1	2	4	8	16	32	64	128
Cross-over	1	2	5	12	28	59	119	240	480	960	1,920
Together	1	2	6	16	46	104	232	475	959	1,922	3,844

From this we have, for the inbreeding coefficients,

$$Z_0 = 0$$
$$Z_1 = 25.00$$
$$Z_2 = 25.00$$
$$Z_3 = 37.50$$
$$Z_4 = 50.00$$
$$Z_5 = 71.88$$
$$Z_6 = 81.25$$
$$Z_7 = 90.63$$
$$Z_8 = 92.77$$
$$Z_9 = 93.65$$
$$Z_{10} = 93.85$$
$$Z_{11} = 93.85$$

These facts will possibly be made clearer to those not actually working much with pedigrees by Table V, which gives the first four ancestral generations[4] of the pedigree of King Melia Rioter 14th.

Generalizing the above reasoning we get the following result.

In A_3, and higher ancestral generations, $2/4 = 50.00$ per cent. of the dam's ancestors are animals which are also ancestors of the sire.

In A_4, and higher ancestral generations, $5/8 = 62.50$ per cent. of the dam's ancestors are animals which are also ancestors of the sire.

In A_5, and higher ancestral generations, $12/16 = 75.00$ per cent. of the dam's ancestors are animals which are also ancestors of the sire.

In A_6, and higher ancestral generations, $28/32 = 87.50$ per cent. of the dam's ancestors are animals which are also ancestors of the sire.

In A_7, and higher ancestral generations, $59/64 = 92.19$ per cent. of the dam's ancestors are animals which are also ancestors of the sire.

[4] In the study of pedigrees stress is naturally laid on the ancestral generations, rather than on the filial, as in breeding experiments. It becomes very convenient to have a brief designation for ancestral generations, in the same way that F_1, F_2, etc., are used to denote filial generations. I would suggest the use of the letter A with sub-numbers for this purpose. We then have A_1 denoting the parental generation, A_2 the grandparental, A_3 the great-parental, etc.

In A_8, and higher ancestral generations, $119/128 = 92.97$ per cent. of the dam's ancestors are animals which are also ancestors of the sire.

In A_9, and higher ancestral generations, $240/256 = 93.75$ per cent. of the dam's ancestors are animals which are also ancestors of the sire.

In A_{10}, and higher ancestral generations, 93.75 per cent. of the dam's ancestors are animals which are also ancestors of the sire.

In A_{11}, and higher ancestral generations, 93.75 per cent. of the dam's ancestors are animals which are also ancestors of the sire.

In A_{12}, and higher ancestral generations, 93.75 per cent. of the dam's ancestors are animals which are also ancestors of the sire.

TABLE V

PEDIGREE FOR FOUR ANCESTRAL GENERATIONS OF KING MELIA RIOTER 14TH

Sex					
♂	♂	No. 63200 ♂ Marjorie Melia Ann's Son.	No. 56581 ♂ Melia Ann's King.	No. 22041 ♂ Melia Ann's Son.	
				No. 100775 ♀ Lottie Melia Ann.	
			No. 157263 ♀ Marjorie Melia Ann.	No. 22041 ♂ ● Melia Ann's Son.	
				No. 905883 ♀ Mary Melia Ann.	
	♀ No. 73104 King Melia Rioter.	No. 181544 ♀ Letty Silver Hair.	No. 58169 ♂ King of All Kings.	No. 54896 ♂ St. Lambert's Rioter King.	
				No. 114804 ♀ St. Lambert's Letty.	
			No. 148456 ♀ Exile's Silver Hair.	No. 32559 ♂ Exile of St. Anne's.	
				No. 60449 ♀ Silver Hair 4th.	
♂ No. 103901 King Melia Rioter 14th.		No. 73104 ♂ ● King Melia Rioter.	No. 63200 ♂ ⊗ Marjorie Melia Ann's Son.	No. 56581 ♂ ⊗ Melia Ann's King.	
				No. 157263 ♀ ⊗ Marjorie Melia Ann.	
			No. 181544 ♀ ⊗ Letty Silver Hair.	No. 58169 ♂ ⊗ King of All Kings.	
				No. 148456 ♀ ⊗ Exile's Silver Hair.	
	♀ No. 262926 Larissa Marie.	No. 219360 ♀ Dula Riotress Maid.	No. 62098 ♂ King Rioter's Lad.	No. 54896 ♂ ● St. Lambert's Rioter King.	
				No. 142296 ♀ King's Riotress Nora.	
			No. 218796 ♀ St. Lambert's Dula Riotress.	No. 57778 ♂ St. Lambert's Boy.	
				No. 174761 ♀ Rioter Lad's First Daughter.	

These percentages are quantities of a good deal of interest. They measure the degree in which King Melia Rioter 14th's sire and dam were related to each other. Community of ancestry is the basis of kinship.

Percentages derived in the way shown above, from cross pedigree elimination tables, I propose to call *coefficients* of relationship, and to designate by the letter K, with appropriate sub-numbers referring to the generation. These relationship coefficients are, with some limitations, independent of the inbreeding coefficients in the values they may take, though the two will usually be correlated to some degree. It is, however, possible to have a high value of Z with $K=0$.

TABLE VI

COMPARING THE MAXIMUM POSSIBLE VALUES OF THE COEFFICIENTS OF INBREEDING (Z) WHEN THE COEFFICIENT OF RELATIONSHIP K EQUALS (*a*) ZERO, AND (*b*) 100

Generation	Maximum Possible Value of Z when $K=0$	Maximum Possible Value of Z when $K=100$
A_1	0	0
A_2	0	50.00
A_3	50.00	75.00
A_4	75.00	87.50
A_5	87.50	93.75
A_6	93.75	96.88
A_7	96.88	98.44
A_8	98.44	99.22
A_9	99.22	99.61
A_{10}	99.61	99.80

The most important feature of the relationship coefficients is found in their genetic implications. This can be indicated best by an illustration. Let us consider the case of the maximum possible degree of inbreeding with $K=0$. This will be found when the sire and the dam are each inbred to the highest possible degree (continued brother $\times$ sister mating) but are in no way related to each other. Such a case would be afforded, for example, if a Jersey bull, the product of continued brother $\times$ sister mating, was bred to a Holstein cow, which was also the product

of a continued brother by sister breeding. Clearly K would be 0, since no animal on one half of the pedigree could even appear on the other. The values of the successive coefficients of inbreeding (Z's) in such a case are shown in Table VI, where they are compared with the coefficients of inbreeding in complete continued brother $\times$ sister mating, where $K = 100$.[5]

From this it appears that an individual may be inbred in 10 generations to within two tenths of one per cent. as intensely, measured by the coefficients of inbreeding, if his sire and dam are in no way related, as he would be if his sire and dam were brother and sister. But clearly the germinal constitution of the individual produced would, except by the most remote chance, be quite different in the two cases. This point is so evident as to need no elaboration. It has been brought out by East and Hayes.[6]

The values of the K's for a particular pedigree evidently furnish a rough index of the probability that the two germ-plasms which unite to form an individual are alike in their constitution. This will follow because of the fact that the probability of likeness of germinal constitution in two individuals must tend to increase as the number of ancestors common to the two increases. Just what is the law of this increase in probability is a problem in Mendelian mathematics which has not yet been worked out. The general fact, however, seems quite sure.

From the above discussion it seems plain that in reaching a numerical measure of the degree of inbreeding it is not sufficient to consider coefficients of inbreeding alone. The coefficients of relationship must also be taken into account.

It is suggested that the two constants be written together for each generation, the coefficient of inbreeding being followed by the coefficient of relationship in brackets. Thus we have

[5] Since, of course, *all* of a sister's ancestors are identical with her brother's.

[6] U. S. Dept. Agr. Bur. Plant Industry, Bul. No. 243, pp. 1–58, 1912.

INBREEDING AND RELATIONSHIP COEFFICIENTS OF KING MELIA RIOTER 14TH

$$
\begin{aligned}
Z_0\,(K_1) &= 0 && (0)\\
Z_1\,(K_2) &= 25 && (0)\\
Z_2\,(K_3) &= 25.00 && (50.00)\\
Z_3\,(K_4) &= 37.50 && (62.50)\\
Z_4\,(K_5) &= 50.00 && (75.00)\\
Z_5\,(K_6) &= 71.88 && (87.50)\\
Z_6\,(K_7) &= 81.25 && (92.19)\\
Z_7\,(K_8) &= 90.63 && (92.97)\\
Z_8\,(K_9) &= 92.77 && (93.75)\\
Z_9\,(K_{10}) &= 93.65 && (93.75)\\
Z_{10}(K_{11}) &= 93.85 && (93.75)\\
Z_{11}(K_{12}) &= 93.85 && (93.75)
\end{aligned}
$$

The physical meaning of these expressions is simple and straightforward. $Z_4(K_5)$ tells us that in the 5th ancestral generation of King Melia Rioter 14th he had only one half as many different ancestors as was possible for that generation, and of his ancestors three fourths were common to his sire and his dam. However one looks at the matter there can be no denial that King Melia Rioter 14th is a closely inbred animal.

In Fig. 1 the heavy broken line gives the relationship coefficients for King Melia Rioter 14th. It will be instructive now to consider another example by way of contrast. Again a Jersey bull, Blossom's Glorene (102701), will be taken. Only the final result need be given.

INBREEDING AND RELATIONSHIP COEFFICIENTS OF BLOSSOM'S GLORENE

$$
\begin{aligned}
Z_0(K_1) &= 0 && (0)\\
Z_1(K_2) &= 0 && (0)\\
Z_2(K_3) &= 12.50 && (0)\\
Z_3(K_4) &= 12.50 && (0)\\
Z_4(K_5) &= 25.00 && (0)\\
Z_5(K_6) &= 29.69 && (0)\\
Z_6(K_7) &= 35.94 && (0)\\
Z_7(K_8) &= 40.23 && (0)
\end{aligned}
$$

The total inbreeding and the relationship curves are given in Fig. 2.

The difference in the breeding of this bull and the one considered in the former example is striking. In the 8th ancestral generation Blossom's Glorene has but 60 per

cent. of the number of different ancestors possible in that generation, but not one single animal in the ancestry of his sire occurs in the ancestry of his dam (within the limits A_1 to A_8). The probability is that Blossom's Glorene is heterozygous in respect of most of his characters, while King Melia Rioter 14th is homozygous.

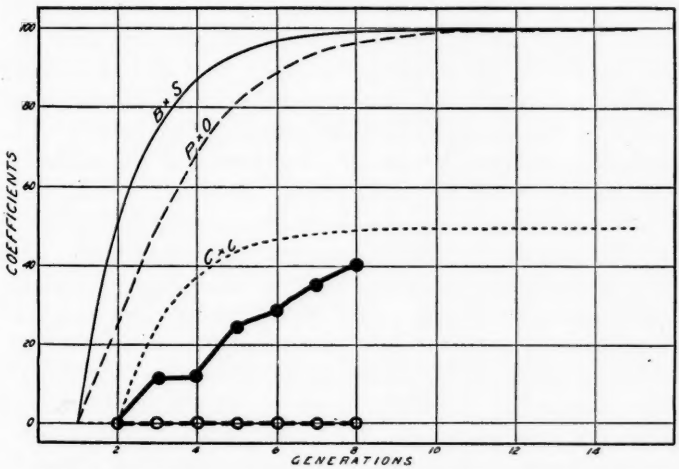

FIG. 2. Diagram showing the total inbreeding (heavy solid line) and the relationship (heavy broken line) curves for the Jersey bull Blossom's Glorene, over a period of eight ancestral generations. Compare with Fig. 1.

SUMMARY

The object of this paper is to call attention to the fact that inbreeding of considerable degree may exist in the entire absence of any kinship between the two individuals bred together, and to bring forward a method of separately measuring what proportion of the observed inbreeding in a particular case is due to kinship of the parents, and what to earlier ancestral reduplication. A proposed coefficient of relationship is described, and its application illustrated by concrete cases.

THE CHROMOSOME HYPOTHESIS OF LINKAGE APPLIED TO CASES IN SWEET PEAS AND PRIMULA

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CALVIN B. BRIDGES

THERE are two views as to the nature of linkage. The earlier view, developed by Bateson and his co-workers, is that this phenomenon is an expression of symmetrical reduplications in the germ tract. A more recent view, developed by Morgan and his co-workers, treats linkage on the basis of a linear arrangement of genes in the chromosomes and of the history of these genes during normal gametogenesis. The advocates of the reduplication view have rarely applied their principles to the results on *Drosophila* on the ground that the results for *Drosophila* are complicated by sex-linkage. That sex-linkage is simply an additional, but wholly independent, phenomenon, is proven by the many cases in *Drosophila* in which sex-linkage is not involved, yet in which the linkage of the genes to each other is of the same type as the linkage of sex-linked genes to each other.

In this paper I shall attempt to show that the theory of linkage which we have successfully applied to all cases in *Drosophila,* whether involving sex-linked genes or genes which show no sex-linkage, applies equally well to the non-sex-linked cases occurring in sweet peas and primula. The only serious drawback to such an application lies in the nature of the data which have been collected for these cases. The least satisfactory form of data from which to determine a linkage value is that presented by F_2 results. In cases in which two recessives enter from opposite parents ("repulsion"), the excessive smallness of the double recessive class in F_2 renders any calculation subject to great error. Slightly better are the F_2 results from coupling,

but here there is no direct parallelism between the zygotic and gametic ratios. In determining what gametic ratio underlies the F_2 results given by an experiment, the practise has been to compare by the eye the given result with a series of F_2 results calculated from selected gametic ratios. Collins has shown[1] that this practise has led to serious error. In F_2 coupling cases in which there has been no crossing over in one sex (autosome genes in *Drosophila*), there is a *direct* relation between the gametic and zygotic series, but only in certain classes which comprise from one fourth to less than one half of the individuals of an experiment. While such data are more accurate than the usual F_2 results, yet the percentage of individuals which can be used directly is so low that we avoid the use of such a method. In F_2 results involving only sex-linked genes, the efficiency is at least 50 per cent., for here there is always a direct relation between the gametic and zygotic ratios in one half the flies (the males). However, half the total number of flies (the females) are useless unless the cross is made in such a way that F_2 becomes a back cross. These different kinds of F_2 results (the two most advantageous of which are not generally applicable) are separated in effectiveness by a wide gap from the back cross which we use equally well in all cases, which gives a zygotic ratio directly proportional to the gametic ratio, and in which *every* individual occurs in the most advantageous relations.

Perhaps the least unsatisfactory method of dealing with such F_2 series as are available in the case of the sweet peas, is by means of the coefficient of association as derived by Yule. Yule's coefficient of association is calculated from a zygotic series of the form $AB:aB:Ab:ab$ by the formula:

$$\text{Coefficient of association} = \frac{(AB \times ab) - (aB \times Ab)}{(AB \times ab) + (aB \times Ab)}.$$

To find the gametic ratio corresponding to this coefficient, use is made of a table which gives the coefficients

[1] AM. NAT., '12.

calculated from the zygotic series corresponding to such gametic ratios as 2.5:1, 3:1, 3.5:1, etc. For the same ratio in the coupling and repulsion series the coefficients are slightly different, so that two tables should be made.

Upon the chromosome basis the best method of expressing the amount of linkage is in terms of percentage of crossing over. The gametic ratio $n:1$ found through the coefficient of association, when expressed as a percentage becomes $\frac{100}{n+1}$.

According to the chromosome hypothesis, all genes which are linked to each other lie in the same chromosome. In sweet peas the first case in which linkage was observed was that of round pollen[2] and red flower color. Later it was found that hooded standard was linked to round and to red. The genes for these three characters, then, may be treated as though carried by the same chromosome, which we may call chromosome I, of the sweet pea.

The relative distances of these genes from one another in the chromosome can be determined from the degrees of linkage. The farther apart in the chromosome any two genes lie, the greater will be the amount of crossing over between them. If two genes lie very close together, then the percentage of crossing-over will be very small (the gametic ratio very large).

Fortunately Punnett has recently collected the data upon these linkage cases in sweet peas. In the table which follows, I have summarized the data given by the various tables of Punnett. In the first column to the right of the data appear the coefficients of association. In the next column appear the corresponding gametic ratios calculated by interpolation to the nearest tenth. In the last column are the equivalent percentages of crossing over, found from the gametic ratios.

We may use one per cent. of crossing over as our unit of distance in measuring the space between two genes.

[2] I have used a terminology here like that used for the cases in *Drosophila*, naming the gene after that member of the pair of allelomorphs which may be considered as the mutant from the wild type of pea.

The gene for red is then about eleven units from that for round, and the gene for hooded is nearly one unit from that for red.

TABLE I

CHROMOSOME I

Round Pollen and Red Color

	Wild Type	Round	Red	Round Red	Coefficient of Association	Gametic Ratio	Percentage of Cross-overs
Coupling	...7,897	583	614	2,197	.9596	7.9:1	11.2

Red Color and Hooded Standard

	Wild Type	Red	Hooded	Red Hooded			
Coupling	...2,568	16	17	857	.9998	125.:1	.8

Round Pollen and Hooded Standard

	Wild Type	Round	Hooded	Round Hooded			
Coupling	... 626	74	83	174	.8932	4.7:1	18.
Repulsion	...3,140	1,413	1,438	14	.9577	8.7:1	10.3

The order of arrangement of these genes in the chromosome can be discovered from a comparison of the linkage values found above. The linkage value (11.2) for round and red is the most accurately determined of those involved, so that we may lay this down as our initial or base line:

DIAGRAM I. R_0 = round pollen, R = red flower.

The next most accurate value is that for red and hooded, namely, 0.8. Hooded lies therefore only about one unit from red, but if these two values only, namely, round red and red hooded, were given, we should be unable to decide whether hooded lies between round and red at a position near 10 (that is, $11.2 - .8$) or beyond red in a locus at 12 (that is, $11.2 + .8$). In order to determine whether hooded lies to the left or to the right of red the data for the third value, round hooded, need only be accurate enough for us to decide between these values of 10

and of 12 units. The data from the coupling experiments (which even though less extensive then those from the repulsion experiments are probably more accurate) give a value of about 18 units. Since the repulsion data give 10 units, 18 is probably too high, and an intermediate position correct. The higher (12) of the two possible values is then the correct value. The position at 10 is not excluded by these data, but is far less probable. In a case in which one of the two first values is very small, as here, the accuracy demanded of the remaining or third value is much greater than in cases where neither of the values are small, and one has only to decide between two very different values by aid of the third. There are other ways of arriving at this order of genes which are independent of the size of the values. One of those methods, such for example, as that of double crossing over, would definitely settle the order of these three genes, but unfortunately such data have not yet been published.

If hooded lies beyond red at 12, the complete first chromosome diagram will be as follows:

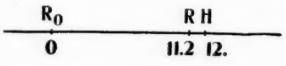

DIAGRAM II. Chromosome I, Sweet Pea. R_0 = round pollen, R = red flower, H = hooded.

In the above diagram R_0 indicates the locus of round (and also of long). The symbols in the diagrams are used to designate loci which may be occupied by either allelomorph of the pair.

It has been observed that hooded flowers have always a uniform color in standard and wings, instead of having these two regions colored differently as in the normal or bicolor type. Bateson assumed that this unicolorism was only another somatic effect of the hooded gene. However, an alternative explanation is that the unicolor is caused by a specific gene which is very closely linked to hooded. If this should be found to be the case, then this fourth gene also will be located at about 12 units from round.

There is one other gene which probably belongs in the first chromosome, namely, the intensifier found in the "black knight" race. The linkage data of red color and intensity of color have been given in Report II to the Evolution Committee, page 90.

TABLE II

Red Color and Intense Color

	Wild Type	Red	Intense	Red Intense	Coefficient of Association	Gametic Ratio	Percentage of Crossovers
Coupling ...	149	29	35	22	.527	1.9:1	35.

If these data are significant, then intense is in the first chromosome at a locus about 35 to the right or left of red. It should give about 24 (35 − 11) or 46 (35 + 11) per cent. of crossing over with round, depending on whether it lies about 24 to the left of round or 35 to the right of red.

The Second Chromosome of Sweet Peas

In the case of the second chromosome in sweet peas, the linkage values are based on smaller numbers, but the order of genes is more certain.

The first linkage case of this chromosome was that of sterile anthers and light axils. Later the cretin form of flower was found to belong to this linkage group. As in the case of the first chromosome, I have summarized the tables of Punnett in Table III.

TABLE III

Chromosome II

Sterile Anthers and Light Axil

	Wild Type	Sterile	Light	Sterile Light	Coefficient of Association	Gametic Ratio	Percentage of Crossovers
Coupling ...	1,170	41	30	379	.9945	22.:1	4.4
Repulsion ..	1,335	643	714	2	.988	20.:1	4.9

Light Axils and Cretin Flower

	Wild Type	Light	Cretin	Light Cretin			
Coupling ...	282	49	52	59	.734	2.6:1	28.
Repulsion ..	48	22	27	3	.610	2.7:1	27.

Sterile Anthers and Cretin Flower

	Wild Type	Sterile	Cretin	Sterile Cretin			
Coupling ...	165	58	58	78	.556	2.:1	33.
Repulsion ..	764	355	345	25	.683	2.6:1	28.

The linkage value for sterile and light, namely, 4.4 units, is the most accurately determined of those in the second chromosome. The value for light and cretin is about 28 units. Using the distance 4.4 between sterile and light as our base line, then, we should find that cretin lies at $4 + 28$ or 32 from sterile if the order of genes is sterile, light, cretin; but if the order is cretin, sterile, light, then cretin should lie at $28 - 4$ or 24 from sterile. The value for sterile cretin should approximate either 24 or 32. There is no very small value here as there was in the first chromosome, and not such great accuracy is required of the remaining value, since it should be easy to distinguish between 24 and 32. The coupling data for this value gives 33 units, which enables us to fix the order of genes as sterile, light, cretin. The following diagram of chromosome II expresses these relations more clearly.

DIAGRAM III. Chromosome II, Sweat Pea. S = sterile, L = light, C = cretin.

When crossing over is as free as in the case of sterile and cretin and of light and cretin there should be some double crossing over. That is, crossing over might occur in the section of the chromosome near sterile and light and at the same time another crossover could occur in the section between light and cretin. This occurrence would be readily seen if normal plants heterozygous in any combination of these three genes were back-crossed to plants purely recessive in all three. A relatively few plants from such a test would give very valuable information on several points, while an experiment of a few thousand individuals from such back-cross tests would enable one to discover, through the phenomenon of interference, much

as to the character of the chromosome, the average length of the internode, and the percentage of chiasmas per node.

Independence of Chromosomes I and II of Sweet Peas

If two groups of genes are carried by separate chromosomes, we may expect to obtain free assortment and typical 9:3:3:1 ratios in F_2, when any two genes from different groups are involved. There are rather extensive data for three such cases in sweet peas, and in each there is practically complete independence. The data given in Table IV are summarized from Report III to the Evolution Committee (page 37) and Report IV (page 17).

TABLE IV

Independence of the First and Second Chromosomes

Round Pollen (1st) and Light Axil (2d)

Wild Type	Round	Light	Round Light	Coefficient of Association	Gametic Ratio	Percentage of Cross-overs
1,246	341	399	142	.131	1.15:1	47.

Red Color (1st) and Light Axil (2d)

Wild Type	Red	Light	Red Light			
1,563	545	506	232	.136	1.16:1	47.

Red Color (1st) and Sterile Anthers (2d)

Wild Type	Red	Sterile	Red Sterile			
838	403	265	147	.071	1.07:1	48.

The greatest departure from the 50 per cent. of crossing over expected from independent assortment is only to 47 per cent.

There are several other characters whose genes seem to be independent of those in the first and second chromosomes. This is interesting from the point of view that each independent gene or group of linked genes requires a distinct chromosome as a carrier.

LINKAGE CASES IN PRIMULA

In the case of primula, linkage was first found between red (versus green) stigma and red (versus magenta) flower color. Long style (versus short) and dark stem (versus light) were found to be linked with red stigma. Indications were observed that still a fifth gene, a dominant which reduces the color of the flower to a tinge in the corolla tube, belonged to this group.

A back cross involving the three genes, red stigma, red flower and long style was made. Credit is due to Gregory for the use of this method for obtaining linkage data. Unfortunately many of the individuals were useless for the linkage of red flower color, because of the occurrence of white; and the numbers are small.

In Table V, I have summarized the data given by Gregory.[4]

TABLE V

THE FIRST CHROMOSOME OF PRIMULA

Red Stigma and Red Flower

	Non-crossovers		Crossovers				
	Red Stigma Red Flower	Wild Type	Red Stigma	Red Flower	Coefficient of Association	Gametic Ratio	Percentage of Crossovers
Coupling back cross	28	39	17	18		1.9:1	34.6
	Wild Type	Red Stigma	Red Flower	Red Stigma Red Flower			
Coupling F_2	1,174	305	289	232	.511	1.8:1	35.3

Red Flower and Long Style

	Non-crossovers		Crossovers				
	Red Long	Wild Type	Red	Long			
Coupling back cross.	40	53	6	5		8.4:1	10.9
	Wild Type	Red	Long	Red Long			
Coupling F_2	38	2	4	12	.966	8.6:1	10.4

Red Stigma and Long Style

	Non-crossovers		Crossovers				
	Red Stigma Long	Wild Type	Red Stigma	Long			
Coupling back cross.	44	64	35	30		1.6:1	37.

[4] *Jour. Genetics*, '11, Vol. I; *Proc. Roy. Soc.*, '11, Vol. —, 84.

		Red Stigma and Dark Stem				
	Wild Type	Red Stigma Dark	Red Stigma Dark			
Repulsion	137	66	62	0	—	—	—

The three values are—red stigma red flower 35, red flower long style 11, and red stigma long style 37. Of these, red stigma red flower is based upon the most data, and may therefore be taken as our base line. The value for red stigma long style should be $35 - 11$ or 24, if the order of genes is long, red stigma, red flower; but $35 + 11$ or 46, if the order of genes is red stigma, red flower, long. The value shown by the table is 37. This means that long lies to the right of red at a locus 46.

DIAGRAM IV. Chromosome I, Primula. R_s = red stigma, R = red flower, L = long style.

58 59 60 61 62

The apparent discrepancy between the values 46 and 37 is due in most part to double crossing over, the effect of which is always to lower large values disproportionately more than short. When the discrepancy is known, the amount of double crossing over can be calculated approximately. Here the amount of double crossing over is

$$\frac{46 - 37}{2} = 4.5.$$

That is, 4.5 per cent. of all the gametes are the result of double crossing over. A somewhat larger amount of data from a back cross in which all the individuals are effective would give by direct experiment a true value for the amount of double crossing over.

A chromosome diagram should be built up of values independent of double crossing over. According to our experience with *Drosophila*, if there is not more than ten per cent. of crossing over between two genes, the double crossing over is negligible. Thus in the first chromosome in sweet peas, the values obtained from the experiments are not changed by double crossing over. However, in the

case of the second chromosome, where the total percentage of crossing over is about 32, there is probably one or two per cent. of double crossing over. The diagram of the second chromosome is in this respect only tentative, and the plotted position of cretin will be moved a little farther to the right when the amount of double crossing over between light and cretin has been found. The value 4.4 for sterile anther light axil is not affected by double crossing over, since the section of chromosome between these two loci is so short that a double break would probably not occur between them at all. The amount of double crossing over between any two loci can only be found when there is a gene between them. Thus if a gene should be found which lies between light and cretin, either by indirect calculation or, better, by direct experiment, the amount of double crossing over could be found. The more genes which can be worked with in the same chromosome, the more accurate becomes the diagram.

All the values found for these cases in sweet peas and primula are based upon such small numbers that they can be used only as illustrations of the way in which one would apply to new cases certain principles worked out in *Drosophila*. While they serve as examples in line with these principles, they are entirely inadequate as proof. A very interesting case of variation in linkage is presented by some of the families involving chromosome II of the sweet pea. In this article I have avoided such data as far as I could, but it is possible that the order in which I have aligned these genes will be found to be incorrect when data upon all three genes in a back cross are obtained. Such data would show, through the phenomenon of double crossing over, what the order of genes is, even though variations in the linkage should occur.

COLUMBIA UNIVERSITY,
May, 1914

THE REDUPLICATION HYPOTHESIS AS APPLIED TO DROSOPHILA

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A NUMBER of papers developing the reduplication hypothesis of linkage have recently appeared in the *Journal of Genetics*. They are based almost entirely on the experiments of Gregory ('11) on *Primula* and of Punnett ('13) on the sweet pea. The data are not entirely satisfactory because of the relatively small number of genes involved, and because in most cases the gametic ratios can be only approximately determined. This is due to the fact that most of the data concern F_2 counts, from which gametic ratios can not be calculated directly. In Gregory's best case a much more satisfactory method was followed—the heterozygous plants were tested, not by mating to others of their kind, but by crossing with plants recessive with respect to all the genes involved, which gives the gametic ratio directly. In this case, however, we have only a relatively small series of data involving as many as three pairs of linked genes. It is obvious that from such data no adequate test of the reduplication hypothesis can be made.

The phenomena of linkage have been very extensively studied, by Morgan and others, in the fly *Drosophila*. In this animal there are many genes belonging to the same linkage groups, and these have been studied on a large scale. In the case of the sex-linked group there is never any difficulty in calculating the gametic ratio from F_2 results, since the F_2 males from any cross always give it directly. I have recently published a paper (Sturtevant, '14) giving a complete summary of the published results obtained from studies of the linkage of these genes. In that paper I have adopted the chromosome explanation of link-

age proposed by Morgan ('11). Here I shall use the same data for a test of the reduplication theory. It may be of value to contrast the two views by making a rigorous application of them to the same facts. Since the data concerning the sex-linked group of genes in *Drosophila* form the simplest and most extensive series now available, I shall deal more especially with them. The reader is referred to my other paper for the detailed data, for references to original sources, and for a full treatment of the chromosome hypothesis as applied to these and other data.

It may be well to give first a brief catalogue of the sex-linked genes discussed in this paper. The nomenclature is that suggested by Morgan ('13). This may be confusing to those accustomed to the "presence and absence" system, but this should not be a serious objection here, since a clear conception of the somatic appearance of the animals discussed is not essential for our present purpose. The relations would be as clear if hieroglyphics were used for symbols.

Y is the gene which differentiates the wild "gray" bodied fly from the yellow mutant, *y*.

V differentiates the wild red-eyed fly from the vermilion-eyed mutant, *v*.

M differentiates the "long" wing of the wild fly from that of the miniature-winged mutant, *m*.

R is another gene affecting the wings. The wild fly has *R*, the rudimentary-winged mutant has *r*.

Br occurs in a dominant mutant form having a narrow eye known as barred. The allelomorph present in the wild fly is designated *br*.

The other characters concerned bear such a relation to one another that the genes involved are considered as forming a system of quadruple allelomorphs. The alternative to this view is the assumption of complete linkage, but I have given elsewhere (Sturtevant, '13) my reasons for preferring the multiple allelomorph interpretation. The eye of the wild *Drosophila* is red in color. A single

mutant obtained from it had white eyes (Morgan, '10), and this character proved to be a simple sex-linked recessive. From the white-eyed form arose a fly with eosin eyes (Morgan, '12). This new character was found to be a sex-linked dominant to white, and a sex-linked recessive to red. Finally, there arose a form with cherry eye color (Safir, '13). This has the same relation to red and to white as has eosin. Mated to eosin it gives an intermediate color, which splits up into cherry, intermediate, and eosin in F_2. The nomenclature adopted in this case is as follows:

Allelomorph present in the red-eyed fly, W.
Allelomorph present in the white-eyed fly, w.
Allelomorph present in the eosin-eyed fly, w^e.
Allelomorph present in the cherry-eyed fly, w^c.

Trow ('13) has suggested the possibility of an asymmetrical reduplication series, giving a gametic series of $wAB:xAb:yaB:zab$, where w need not equal z, nor x equal y. It should be noted that an actual demonstration of such a ratio, or of its non-existence, is almost excluded for the reason that it would be practically impossible to be sure one was not dealing with a case involving differential viability. However, perhaps the most striking general fact brought out by the study of linkage is that each pair of linked genes (allelomorphs), considered separately, follows a perfectly regular Mendelian course. I think we are, therefore, justified in assuming that the number of gametes bearing A is always equal to the number bearing a, and similarly for B and b. Then, in Trow's asymmetrical series,

$$w + x = y + z,$$
$$w + y = x + z.$$

Hence,

$$w = z \quad \text{and} \quad x = y.$$

In all that follows I shall assume that the reduplication series are always symmetrical. On this assumption it becomes unnecessary to consider the two halves of the

series separately, and I shall therefore use only two terms in speaking of gametic ratios. By adding together the two halves of the series larger numbers are obtained, so that chance deviations are relatively smaller. Differential viability is also partially overcome in this way. Of course on the reduplication theory both terms of the gametic ratio must be integers, since they represent numbers of cells, but nevertheless it has seemed to me more convenient for purposes of calculation to express them always in the form n:1. Thus a gametic ration of 3:2 may be written 1.5:1.

It was suggested by Bateson and Punnett ('11) that the intensity of coupling and of repulsion between the same two pairs of genes may be identical. That this is substantially the case has been shown again and again in *Drosophila,* and has become a truism among those working on that form. Before presenting data on this point I wish to bring up another matter on which the same data have a bearing. Punnett ('13) has said, "But where three [pairs of] factors are concerned . . . the value of the primary reduplications is evidently altered, and there would seem to be some process whereby these reduplications react on one another." Bailey ('14) has suggested that the nature of this interaction may be such as to cause the two primary series to be of equal intensity. It may be categorically stated that *there is no interaction effect in Drosophila.* The best data for a test of the relative intensity of coupling and repulsion, and of "fundamental," "primary" and "secondary" reduplication series, involving the same allelomorphic groups, is that furnished by the relations of the various forms of W (W, w, w^e, w^o) to the M pair of allelomorphs (M and m). Table I is a summary of the data on this case. In computing the fundamental series I have used only the data from such of my own experiments as involve only two pairs of genes, since that from other sources is for the most part made up of primary series in which the other primary series involved is masked.

TABLE I

FUNDAMENTAL SERIES

Nature of Cross	Actual Numbers	Gametic Ratios
$WM \times wm$	777: 470	1.6 +: 1
$Wm \times wM$	93: 221	1: 2.4 —
$WM \times w^e m$	634: 348	1.8 +: 1
$Wm \times w^e M$	46: 110	1: 2.4 —
$Wm \times w^e M$	461: 855	1: 1.9 —
$w^e M \times wm$	4,171: 1,858	2.2 +: 1
$w^e m \times wM$	891: 1,898	1: 2.1 +
$w^e M \times wm$	75: 47	1.6: 1

PRIMARY SERIES

Nature of Cross	Actual Numbers	Gametic Ratio	Other Primary Series Involved
$WM \times w^e m$	178: 85	2.1 —: 1	MBr'
$w^e m \times wM$	69: 122	1: 1.8 —	MBr'
$WM \times wm$	5,838: 2.911	2.0 +: 1	YW
$Wm \times wM$	1,111: 2,493	1: 2.2 +	YW
$WM \times wm$	2,261: 1,011	2.2 +: 1	MR
	Secondary Series		Primary Series
$WM \times w^e m$	719: 407	1.8 —: 1	WV, VM
$Wm \times w^e M$	227: 509	1: 2.2 —	WV, VM

It will be noted that in all these cases the gametic ratio approximates 2:1, or 1:2, according to the nature of the cross. There are only four cases showing a noticeable deviation from this value, and of these two involve only small counts. The most serious is the first. In this case there is a deviation of 54.3 from the 2:1 ratio, and the standard error is $16.7[\sqrt{1/3 \times 2/3 \times (777 + 470)} = \pm 16.7-]$. Since the deviation is slightly over three times the standard error, it is perhaps significant, especially since there is at least one other rather large deviation (the second ratio in Table I). For our present purpose, however, it is probably not significant, since similar deviations occur in different experiments of exactly the same type. I have recorded elsewhere (Sturtevant, '14) the results of a number of tests of individual females heterozygous for these two allelomorphic groups. Taking only those cultures which produced 100 or more flies, we find the following results:

Seven females of the constitution $w^e mwM$ gave gametic ratios ranging from 1.5:1 to 2.7:1, with the modal class at about 2.0:1.

Seventeen females $w^e Mwm$ gave ratios ranging from 1.5:1 to 3.4:1, with a single individual at 4.2:1. The modal class was at about 2.2:1.

It seems highly probable that all these deviations from a 2:1 ratio, not due to insufficient numbers, may be satisfactorily explained on the basis of differential viability, which is known to occur here (for a discussion of the vagaries of differential viability see Bridges and Sturtevant, '14). I do not wish to be understood as arguing that the gametic ratio for any two pairs of genes is absolutely constant, but only that it is in most cases uninfluenced by the way in which the genes are combined and by heterozygosis for other genes. That it may sometimes show marked differences is now well established. I have myself studied two cases of this sort, and I have good evidence (not yet published in detail) that there are definite genes which cause great differences in the gametic ratios for whole linkage groups. In one case this gene itself shows linkage to those in the group it affects. But even here the intensity of coupling and of repulsion is affected alike, and it makes no difference how few or how many genes a fly is heterozygous for; the linkage is strong or weak according to the form of the linkage-affecting gene which the fly happens to carry. In each of these cases I have been able to obtain about the same extreme values both for coupling and for repulsion.

In what follows I shall assume that the intensity of the reduplication series is not affected by the way in which the genes are introduced, nor by the number of linked genes involved in the cross. The obvious corollary of this is that reduplication occurs even in homozygous individuals, and that the nature of the series of divisions is in general independent of the constitution of the individual. This conclusion is directly opposed to the point of view expressed more especially by Punnett, in the

passage quoted above and elsewhere. If reduplication occurs at all it is the same in the wild fly as in the most complex linkage experiment we have yet carried out.

If it is assumed that the intensity of coupling and repulsion is identical, it becomes unnecessary to consider them separately. I shall therefore lump together all the data involving the same groups of allelomorphs, regardless of how they were put into the cross. When three pairs of genes are involved there are eight possible combinations of them in F_2, but only four if we add together the two halves of the reduplication diagram. There are the two original combinations, which I shall designate *ABC*. Then there are three combinations derived from each of these by a shifting of one gene, which I shall designate *ABc*, *AbC* and *aBC*, the small letters referring to those pairs which have been shifted. Thus, to take an imaginary case, if we cross *LMn* by *lmN*, the gametes produced by the F_1 individuals will be classified as follows:

ABC	*ABc*	*AbC*	*aBC*
LMn	*LMN*	*Lmn*	*lMn*
lmN	*lmn*	*lMN*	*LmN*

In the following tables I shall reduce all data to this form. In each case the genes will be arranged so that *AB* and *BC* will be the primary reduplication series.[1]

Table II contains such a summary of all the crosses involving three pairs of sex-linked genes. Table III shows the gametic ratios derived from these data, and also the values for the secondary series calculated on the basis of Trow's "special" hypothesis. For the sake of brevity only one term is used: a gametic ratio of 3:1 is written 3; a ratio of 3:2 becomes 1.5, etc. With the simplifications introduced here Trow's formula becomes

$$AC = \frac{(AB \times BC) + 1}{AB + BC}.$$

[1] As was pointed out by Punnett ('13), in a system of three reduplication series the one with the lowest intensity is to be regarded as the secondary series.

TABLE II

Allelomorphic Groups	*ABC*	*ABc*	*AbC*	*aBC*
YWM	8,212	4,013	9	119
YWR	278	160	0	1
YVM	1,082	58	22	665
YVR	315	138	55	196
YVBr'	93	34	10	54
WVM	194	11	1	102
WMR	1,726	535	139	872
WMBr'	220	73	25	129

TABLE III

Experiment	Gametic ratios			
	Observed			Calculated
	AB	*BC*	*AC*	*AC*
YWM	95.5	2.1	2.0−	2.0+
YWR	438.0	1.74	1.72	1.74
YVM	1.7	22.0	1.5	1.6
YVR	1.8	2.6	1.1	1.3
YVBr'	2.0	3.4	1.3	1.4
WVM	2.0	24.7	1.7	1.9
WMR	2.2	3.9	1.3	1.6
WMBr'	1.9	3.6	1.2	1.4

It will be seen that in every case the calculated value for the secondary reduplication is higher than the observed value. The same relation comes out in two experiments which I have done involving genes of another group in *Drosophila* (see Table VIII, Sturtevant, '14). Punnett's case is so involved that calculations accurate enough for our present purpose can not be made. In Gregory's experiment one of the genes (*M*) could not be followed in all the plants because masked by another gene. We are not given the data for *S* and *G* in those plants in which *M* was classified separately from those in which it was not. The data are therefore not available for exact calculations, since the numbers are too small to overcome chance deviations. The data for my own two experiments appear in Table IV.

The same relation comes out more strikingly in another way. If we let *m* equal the intensity of the *AB* series and *n* that of the *BC* series, then on Trow's special hypothesis

the four kinds of gametes should occur in the following proportions:

$$ABC - mn$$
$$ABc - m$$
$$aBC - n$$
$$AbC - 1$$

TABLE IV

Experiment	Observed			Calculated
	AB	*BC*	*AC*	*AC*
BVgCv	3.4	11.6	2.4	2.7
BCvSp	2.5	2.1	1.0	1.4

That is, $1/(m+1)$ of the gametes should have A and B interchanged. Of these, $1/(n+1)$ should have B and C also interchanged. If N represents the total number of gametes, then the size of the AbC class should be represented by the expression

$$AbC = \frac{N}{(m+1)(n+1)}.$$

Table V shows the relation between the size of this class as observed and as thus calculated, in the ten experiments.

TABLE V

Allelomorphic Groups	*ABC*	
	Observed	Calculated
YWM	9	42
YWR	0	0
YVM	22	30
YVR	55	69
YVBr'	10	15
WVM	1	4
WMR	139	208
WMBr'	25	34
BVgCv	2	7
BCvSp	12	20

Thus it appears that in all ten experiments Trow's formula gives values for the AC series and for the AbC

term which are too large. Moreover, this feature appears in a more complex cross which I have carried out, involving four pairs of linked genes (*YWVM*), and in each separate part of all these experiments, regardless of how the crosses were made. It may, then, be taken as a constant relation. It can only mean that there is some relation between *A* and *C* besides that resulting from secondary reduplication. In other words, to use Bailey's terms, Trow's "special" hypothesis is not valid.

Let us then examine what Bailey calls Trow's "general" hypothesis. Suppose the primary series to be of the following values:

$$AB = l:1,$$
$$BC = m:1,$$
$$AC = n:1.$$

Trow's general formula for calculating what should be the observed value of the *AC* series is

$$AC = \frac{lmn + n}{l + m}.$$

The special formula is derived from this by assuming $n = 1$, when the formula becomes

$$AC = \frac{lm + 1}{l + m}.$$

Since this always gives a value which is too large, it follows that n is always less than one. This means that the *AC* primary series is reversed—that the combinations present in the parents tend to be reproduced in fewer numbers than the new combinations. I have worked this out for the case of *BCvSp* (see Table IV), and find the primary series there to be 0.6:1, though the observed series is 1.0. The "fundamental" *AC* series has been obtained for most of the cases in Table III, and has always been found to be of the usual form (*i. e.*, n:1,

where $n > 1$). (See Table I, Sturtevant, '14.) In fact, as stated above, the fundamental series always approximates the secondary (observed) series.

There are two hypotheses as to the mechanics of reduplication series where more than two pairs of genes are involved. The first was suggested by Bateson and Punnett ('11), and consists in the assumption that when three pairs are involved eight cells are formed by three successive divisions, each of which segregates one pair of genes. The eight cells then represent the eight possible kinds of gametes, and are supposed to reduplicate independently until the proper proportions are reached. Bailey supposes that if it be shown that two primary series do not interact on each other this scheme will be more likely to be correct than will Trow's, which I shall discuss next. It seems to me, however, that this hypothesis begs the question. It is derived entirely by working backwards from the observed results; it affords no basis for predictions; and it does not offer a simple mechanical explanation of any of the observed results. For pragmatic reasons I believe we should adopt it only as a last resort.

Trow supposes that two cell divisions occur, segregating two pairs of genes. The four resulting cells then go through with their reduplication, which is a primary one. When this is finished there occur divisions which segregate the other pair, and the other primary reduplication is carried out. On Trow's general hypothesis, which I have tried to show is the only one which can hold, it is supposed that the second series of reduplications is affected by both of the first two pairs of genes. *C* is reduplicating more if with *B* than if with *b*, less if with *A* than if with *a*. This scheme of Trow's has one great advantage in that it accounts for the fact that the class which I have called *AbC* is always the smallest one. Reference to Trow's calculations will show that this relation should always occur, and Table II shows that it does occur. On the octant scheme there is no explanation of this relation—we simply have to assume that it does occur somehow.

It will be noted that several of the gametic ratios involved here closely approach 2:1. *YV, YM, WV* and *WM* are the most conspicuous examples. It may seem that such a simple ratio is due to a very simple reduplication series, but I do not think such an assumption can be successfully maintained. The tables given above show that *YM* and *WM* have approximately this same value when they appear as secondary series, and the data for the combination *YWVM* show the same thing for *YV* (see Sturtevant, '14).

If, as I have maintained above, the same series of reduplications must occur in all flies, whether we can follow it or not, then it follows that in these three cases the 2:1 ratio is never due to a simple series, but always to a long and complicated one, since in all three one of the primary series is of high intensity.

It was pointed out by Trow that the intensities of the reduplication series afford a method of calculating the number of cell divisions necessary to complete the series. If we assume that approximately the same series is occurring both in homozygous and in heterozygous flies, we have the following series in *Drosophila* as a basis for such calculations.

Sex-linked Group

$YW = 90.1$
$WV = 2.1$
$VM = 31.8$
$MR = 5.0$
$RBr = 21.7$

Second Group

$BVg = 3.6$
$VgCv = 10.4$
$CvSp = 2.8$
$SpBa = 10+$

Third Group

$PEb = 100\pm$

All of these series must be considered as either primary or secondary and therefore involving primaries of higher intensity. In fact there is unpublished evidence that many of them can not be simple primaries. A number of series of very high intensity are known, and will appear in future publications. Therefore all the calculations that follow give results which are far too small.

According to Trow, the minimal number of successive cell divisions required to complete the series is given by the expression $mnp \cdots$ where m, n, p, etc., are the larger terms of the primary series involved. In the present case the value of that expression is something over 76,000,000,000. However, Trow's formula seems to be wrong. If a be the number of cell divisions required to produce m cells, then $2^a = m$. If this expression gives a value of a which is not an integer, then the next higher whole number is to be taken. In the case of the first series two divisions are necessary to segregate the genes, and in the following series one is required. The number of successive cell divisions required then is $(a+1)+(b+1)+(c+1)+\cdots+1$, where b, c, etc., bear the same relation to n, p, etc., that a does to m. In the case of *Drosophila* the value of this expression is 56. As pointed out. however, this value is certainly far too small.

The total number of cells required is given by the expression $2mnp \cdots + 2np \cdots + 2mn \cdots + 2mp \cdots + 2m \cdots + 2n \cdots + 2p \cdots + \cdots + 2mnp + 2mn + 2mp + 2np + \cdots + 2m + 2n + 2p + 1$.

This gives a value considerably above 600,000,000,000—a manifest absurdity. However, it is not necessary that all these cells should be produced, since the ratios would not be appreciably affected by some lines becoming crowded out. It is necessary, on the other hand, that all of the series shall be completed in every line which does live, since every female *Drosophila*,[2] which is of the proper constitution to be tested, shows linkage for every pair of genes tested.

[2] The results discussed here deal only with the linkage in female flies.

Thus we are forced to assume an enormously complex series of cell divisions, many of them differential, proceeding with mathematical regularity and precision, but in a manner for which direct observation furnishes no basis. It seems to me that it is not desirable to assume such a complex series of events unless we have extremely strong reasons for doing so. I can see no sound reason for adopting the reduplication hypothesis. It apparently rests on two discredited hypotheses: somatic segregation, and the occurrence of members of the 3:1, 7:1, 15:1, etc., series of gametic ratios in more cases than would be expected from a chance distribution.

The chief advantage of the chromosome hypothesis of linkage which has been proposed by Morgan ('11), and which I have followed elsewhere, seems to me to be its simplicity. In addition it appeals to a known mechanism, and a mechanism toward which the experiments of Boveri, Herbst, Baltzer and others point as the correct one. It explains everything that any of the forms of the reduplication hypothesis does, and in addition offers a simple mechanical explanation of the fact that "secondary series" are always smaller than Trow's "special hypothesis" calls for them to be. On the reduplication hypothesis this fact must merely be accepted, for, I think, it can not be explained.

COLUMBIA UNIVERSITY,
May, 1914

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PATTERN DEVELOPMENT IN MAMMALS AND BIRDS. III

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PARTIAL ALBINISM IN WILD BIRDS

In birds under natural conditions of wild life partial albinism is fairly common. Lists of species of which albinistic specimens are known were published by Ruthven Deane (1876, 1880) some years ago, and by others. Scattered instances are in all the bird journals or magazines of general natural history. In most cases in which the white markings are clearly defined against the pigmented parts of the plumage, these may be referred to their particular primary breaks between the several areas of pigment formation. In other cases the pigment reduction is of the diffuse type, tending to form spots.

A few instances follow in which the several primary patches have been observed in wild birds, either as accidental marks or as permanent parts of the pattern.

The Crown Patch.—In 1908, a pair of robins nested near Lowell Park, Cambridge, one of which showed a partial separation of the crown patch, through the presence of a white band, as broad as the eye's diameter, passing from one eye around the back of the head to the other eye. In the *Wilson Bulletin* (Vol. 2, p. 45, 1908) W. E. Saunders records the capture of two robins each with a white collar about the neck, probably marking the separation of the neck patches from the shoulder patches. Coues (1878) records a brood of *black* robins at St. John's, N. B., one of which was kept in captivity by the late G. A. Boardman. In September, after moulting, it was still pure black, except for white wings and tail, which seems to indicate an areal restriction of the shoulder and rump patches, though the pigment, where

produced, must have been superabundant. Ward (1908) has described a case of a black robin becoming albinistic and reviews a number of such cases. The ability of the same feather follicles in different moults to produce feathers with different sorts or amounts of pigment is thus evidenced and has lately been carefully studied by Pearl and Boring (1914) in the hen.

In addition to the case of the robin above mentioned, the white line marking off the crown patch from the ear patches is sometimes found abnormally in other birds. Thus Sweet (1907) records two slate-colored juncos (*Junco hyemalis*) taken in March, 1903, at Avon, Maine, in which there was a white line above the eye, and the black throat patch was absent, owing no doubt to the ventral restriction of the neck patches, as often seen, for example in pigeons. Maynard[1] figures the head of a young female black-poll warbler (*Dendroica striata*) in autumn, showing an inclination to assume a white superciliary stripe. I am convinced that this mark so common in many birds, is merely a development of the primary break marking off the crown patch from the ear patches so that it has become a permanent part of the pattern.

The failure of the crown patch to develop at all, as is sometimes the case in the domestic pigeon, results in a white-crowned bird. In the West Indian *Columba leucocephala,* exactly this modification has taken place and the entire top of the head is permanently white. The same condition is found in sundry other genera, including a humming bird, a heron, and others. It would be interesting to discover by experiment if it were not easier to produce a definite white marking through selecting for the non-development of a certain patch or patches, than to try to restrict a certain pigment patch to definite bounds as in the experiments of Dr. MacCurdy and Professor Castle (1907).

The crown patch as a separate unit in pigmentation, is often of a different hue from the surrounding patches.

[1] "Birds of E. North America," 1896, p. 585.

Thus in the case of the terns, the black-capped chickadee, the black-crowned night heron, and other birds, a black crown patch is noticeably marked off.

The Ear Patches.—The ear patches in birds are small, yet often specially marked out by white boundaries, which are permanent parts of the pattern. Yet there is no doubt but that the acquisition of such white boundaries is a derived character. It is common for the ear patches to be colored differently from the surrounding parts, forming as in some species of tanagers a black auricular area contrasted with the blue of the head and neck. Of particular interest in the present connection, however, are those cases in which a pigmented ear patch is more or less clearly marked off by a white line above it or below, or both. The superciliary stripe, so common in birds, is of course a development of a primary break above the patch, separating it from the crown patch. Where the stripe is narrow it is hard to say which patch has begun to be restricted, though often no doubt both are more or less involved. Thus the Garganey teal has a very wide white eye stripe, and in other species of ducks the whole side of the head may be white, indicating much greater restriction of pigment formation in contiguous patches. A beautiful example of the development of a white stripe at the *lower* border of the ear patches is found in the Inca tern, in which a line of white feathers runs from just above the gape along the lower side of the auricular patch and separates it from the dark throat. But not only is the white line developed, but the feathers composing it are specially elongated and recurved, as if the mark were one of particular decorativeness. The dark ear patch is noticeable in many hawks, separated above and below by white areas, as in the duck hawk and the osprey, though differing in the size of the white areas.

An instance in which the white line separating the crown patch from the ear patch, is even now in course of becoming established as part of the permanent pattern,

is afforded by the common guillemot (*Uria troille*) of the northern Atlantic. The other related species of the genus have the head and neck uniformly pigmented, but in *U. troille* a considerable proportion of specimens show a narrow white eyebrow and a postorbital line, in exactly the situation of the stripe in the albino robin previously noted, though not so broad nor so extended. Birds so marked were formerly considered a distinct species—the ringed murre (*Uria "ringvia"*)—or perhaps a plumage of *U. troille,* and much effort has been made to determine their exact status. Both plumages are found in the same colonies and the two sorts of birds are known to have mated together (Müller, 1862). Verrill estimated that about 40 per cent. of the nesting birds he saw on the Labrador coast were of this variety, but this is probably a rather high estimate. I am convinced that the true explanation of this puzzling variation is that incipient albinism has gained a foothold, of such nature that areal restriction of the ear or crown patches is developing, so that a white line results between them. In the crested auklet (*Æthia*) a member of the same family, of the Pacific Coast, such a line has become fixed so that it now forms a characteristic mark of the species. In the case of the "ringed murre," I should expect to see the eye stripe in the young as well as in the adult stage of those individuals which are to have the mark—in other words it is a permanent trait. No doubt the heredity of this white stripe is of some definite sort, and if a recessive character, it may nevertheless in time become common to an increasing number of birds, as this is a colonial species and the possibility of inbreeding is thus increased.

The Neck Patches.—In birds the neck patches extend forward from the breast to meet the crown patch at the occiput and the ear patches at the sides of the head, thence ventrally to include the throat and chin. A study of albinistic pigeons, as previously noted, indicates that the neck patches are two separate areas of pigmentation,

one on each half of the part covered, with an ultimate center at the base of the neck, usually the last spot to remain when the area is much reduced.

In albinistic individuals, that is, those in which restriction of the pigment areas has taken place, the neck patches are usually first reduced at the upper part of the throat, so that a white patch appears from the chin to upper throat, as commonly seen in street pigeons; in others, however, the restriction may be at the posterior end of the patch, so that a white ring develops at the base of the neck.

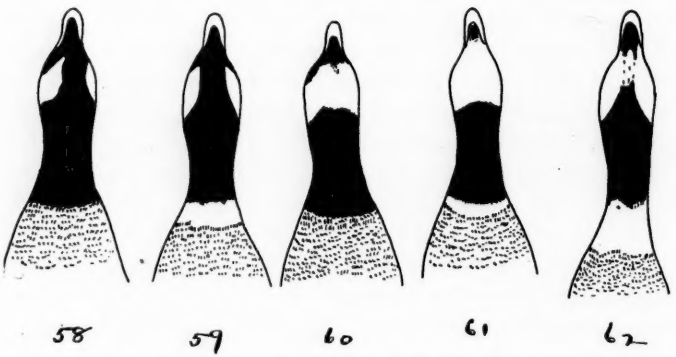
In many birds the neck patches have been much developed as characteristic pigmented areas. Two general categories may be here distinguished: (1) those in which the neck is rather uniformly colored all about, and (2) those in which the ventral portion is heavily pigmented and the dorsal portion much less so. In the latter belong such birds as the black-capped chickadee (*Penthestes atricapillus*) with a black throat but a pale neck. So, too, the golden-winged warbler (*Vermivora chrysoptera*). In this latter category it is probable that a second factor is present, comparable to that producing a centrifugal type of pigmentation in mammals, such for example as in the Himalayan breed of rabbit, which has the end of the nose and the feet black-pigmented, contrary to the usual rule of normal areal reduction where the extremities are the first to become white. That this is a separate category from a physiological standpoint is indicated by its behavior in heredity as worked out so admirably by Faxon (1913) in the case of the Brewster's warbler. He discovered that the black throat as present in the golden-winged warbler is recessive in the cross with a related species, the blue-winged warbler (*Vermivora pinus*), a yellow-throated bird. The offspring of this cross have white throats,—the so-called *V. leucobronchialis*. The black throat patch may be evidence of "centrifugal" pigmentation as defined farther on (p. 53). The essential bilaterality of such a throat patch is

further shown by the fact that one half only may be present as in the golden-winged warbler recorded by Dr. C. W. Townsend (1908).

The first category, in which the neck is uniformly pigmented is illustrated by many of the duck tribe, and probably involves the normal primary patches only. The primary patches are usually restricted first anteroventrally producing a white throat. Often this is carried dorsally so as to form a white ring around the upper part of the neck by the separation of the neck patch from the crown and the ear patches. Again, if the neck patches are restricted posteriorly a white ring is formed at the base of the neck, a common permanent character in many species. The peculiar little goose-like bird—*Nettapus,* of India—has developed this type of marking so that its white neck is encircled by a narrow black ring, and the Labrador duck (*Camptorhynchus*) has a nearly similar mark (Fig. 57). Other ducks, *e. g.,* the mallard, have the white ring at the base of the neck, only.

In an interesting paper on the geese occurring in California, Swarth (1913) has pointed out that in the cackling goose (*Branta c. minina*) there is much variation in the amount of white on the head and neck. Figs. 58 to 62 are traced from a series of photographs illustrating this paper and show the throats of five specimens. The wide range of variation in these specimens indicates to my mind that this goose is in process of reducing the neck patches, and thereby developing a white collar, such as is present in the mallard, and perhaps also a white throat. The usual condition seen in *Branta canadensis* and in so-called normal specimens of *B. c. minina* is seen in Fig. 58. The white cheeks have been developed long ago in the history of the species, in part perhaps by the depigmentation of the ear patches. Now a second change is taking place in one of its subspecies. Thus in Figs. 59, 61 and 62, the neck patches have been reduced posteriorly, a varying amount in each case. In Figs. 60, 61 and 62 these patches have been restricted anteriorly pro-

ducing a white throat, and as sometimes in the pigeon, imperfectly, so that a little island of pigment is cut off just at the chin. It is also obvious from these figures, that reduction may take place either at one end or the other, or at both ends in different individuals. The ultimate development of this line of reduction will produce



FIGS. 58–62. VARIATIONS IN THE DEVELOPMENT OF THE NECK PATCHES IN THE CACKLING GOOSE (after Swarth).

the narrow black collar seen in *Nettapus* previously mentioned. It is worth noting also that in this goose the limits of the neck patch are by their black color sharply defined posteriorly from the gray of the breast which is pigmented from the shoulder patches.

The Shoulder Patches.—The shoulder patches appear to center near the base of the wing, and in reduction produce white remiges, such as appear in a domesticated race of guinea fowl, as well as a white breast. The domesticated guinea fowl often shows this white area in the midline of the breast as the pigment areas fail to spread ventrally. In the normal pattern of wild birds, however, white wings are seldom seen except among certain sea birds. White wing patches are often developed, but these are frequently only bars on pigmented feathers as in the goat-suckers. Probably among small land birds much white in the large wing feathers is a disadvantage,

and so not much developed. It is noticeable that white patches in the wing are often of such a nature that they are concealed through the folding of the wings when the bird is at rest. This accords with my belief that while in flight the bird is unavoidably conspicuous by reason of its motion, and that white patches showing at such times add little or nothing to the disadvantage. In the hairy and the downy woodpeckers (*Dryobates*), a white stripe down the back is developed as part of the pattern, and no doubt as in many mammals, marks the separation between the pigment areas of opposite sides. Centrifugal pigmentation is seen in some species as the kittiwake in which the *outer* primaries are black.

The side patches are commonly continuous with those of the shoulders, and when ventrally restricted, give a white abdomen. Their median separation dorsally, is seen in the hairy and downy woodpeckers as above noted. I have not studied any special developments of these areas, and they are commonly small.

The Rump Patches.—In birds as in mammals the two rump patches pigment the posterior extremity of the body. Their ultimate centers are dorsal and so close together that it is much less common for them to be separated medially than to be restricted laterally. With a slight areal reduction, a separation takes place between them and the side patches dorsally, so that a white area on the rump results. Often this white area represents doubtless a slight restriction of both sets of pigment patches which by drawing farther apart increase the white area along the lower part of the back. In the domestic pigeon much variation may be found, from a condition in which the lower back is wholly pigmented to one in which it is mostly white. The primary break which causes this white patch has been much developed in many groups of birds as a particular mark in the pattern. In many species it is simply of a paler hue than the surrounding parts as in the yellow-rumped warbler (*Dendroica coronata*) or the pine grosbeak (*Pinicola*).

In others the tendency to albinism thus expressed has gone farther so that a pigmentless spot is formed. This white rump patch is present in many unrelated groups of birds in which it has independently arisen through parallel development. Thus it is seen in many of the smaller petrels, in the palm swift, the flicker woodpecker, the white-rumped and other sandpipers, the white-rumped shrike, the European house martin and others. The tail feathers are pigmented by these patches, and among various species show many steps in the process of pigment reduction. As in the domestic pigeon, occasional albinistic individuals show white outer tail feathers, in accordance with the rule that the first pigment reduction takes place at those parts of the primary areas that are farthest removed from the pigment centers. I have seen a white outer tail feather in wild specimens of song sparrows and Lincoln's sparrow and it is occasional in other species. In others again this mark has become developed and fixed as a species character. Thus in the bay-winged bunting (*Poœcetes gramineus*) there is a single white outer feather on each side, in the junco (*Junco hyemalis*) there are two. A white central tail feather is much rarer, but a pure white tail is found occasionally as in the hummingbird, *Leucuria phalerata,* the bald eagle and certain gulls, due to the permanent reduction of the pigment area of the rump at this extremity. I once examined an albino ruffed grouse (*Bonasa*) which was entirely white except for a single feather among the upper tail coverts at the left side of the rump. This blemish in the otherwise pure white bird seemed inexplicable to those who examined it with me, but it merely represents the last remnant of the left-hand rump patch, still persisting though all the other pigment centers were inactive.

It is very interesting that the white rump mark, so commonly found in unrelated groups of birds, is one which is conspicuous in flight only, and the same is true of many of the white tail marks, such as outer white

feathers that disappear when the tail is shut. This points to the conclusion that the development of a white mark which is ever conspicuous is allowed in nature in such cases only where it may be no detriment to the species through rendering it too conspicuous by contrast. Thus the bald eagle or the black-backed gull have nothing to fear from such a banner mark. For small weak-flying birds, however, the case may well be different. Yet even these often show much white and I believe that it would be possible for a species in its phylogeny to develop more and more white if at the same time its habits of watchfulness or other actions developed equally to counteract any disadvantageous result that might accompany the increase. No doubt also a psychic factor is involved, comparable to what among ourselves we call "fashion." Thus a change in action or dress which departs too far from the accustomed appearance is apt to be disliked at first, though in time it may if persisted in, be tolerated and at length accepted. In the development of white markings, for example in the feathers of the tail, it seems likely that a series of small steps must have been made rather than too great and sudden changes. So in the rock pigeon the white of the tail is limited to the outer vane of the outer tail feather. In the turtle dove the outer vane of the outer feather, and the entire tips of the four outer feathers are white. The next step would be to develop an entirely white outer feather and then two (as in the passenger pigeon) and so on. In the sparrows similar steps are shown by the lark sparrow (*Chondestes*) in which the tips only of the outer feathers are white, the bay-winged bunting which has practically all the outer feather white, and a little of the tip of the second, the junco with two outer feathers and part of a third white. No doubt steps such as these must have been passed through by many white-tailed species.

It is difficult to say how disagreeable to their normally colored neighbors, albino birds may be. I have seen an albino robin in the fall of the year with a flock of other

robins and a white-spotted bee-eater with a flock of its brethren, in both cases wholly at peace. This of course was in flocking time when the social spirit is strong. The song sparrow (*Melospiza*) with white outer tail feathers, previously mentioned, was attacked and driven off by another song sparrow. In the *Journal of the Maine Ornithological Society* (Vol. 6, p. 48, 1904), C. H. Clark writes of a pair of albino eave swallows (*Petrochelidon lunifrons*), at Lubec, Maine,

> among a large colony of the common ones who seemed greatly annoyed at the albinos' presence and fought with them until they finally killed one . . . or rather injured it so badly that it died soon after.

I also have a note of a white robin at Montclair, N. J., which in early July, 1909, was seen to be much beaten and driven about by another robin and eventually flew at full speed against a tree and was killed.

CENTRIFUGAL COLORATION

In addition to the primary pigment patches which I have discussed at some length, and the speckled condition or "English" marking, there is, as I have already intimated, a third condition in which pigment is developed at the extremities or points. It may be called a *centrifugal* type and is almost the reverse of the *centripetal* or "primary-patch" class.

The two latter types of pigmentation may both be found in the same individual, but ordinarily this is not evident except in cases where the primary patches are somewhat restricted in area. It then may become apparent that pigment is present at exactly those points where, in the centripetal type of coloring, it is first to be lacking. Moreover it persists strongly, even though the primary areas are much reduced or largely absent. Curiously this sort of pigment seems almost always to be *black*. Apparently centrifugal pigmentation does not occur in all species. I have never seen any trace of it in dogs. In the house cat it is frequent, however. Thus in Figs.

18 and 19 it appears at the end of the tail. In the former figure the sacral patches are much reduced, though present, and together spread nearly half the length of the tail. The terminal half, or less, of the tail, however, is dark-pigmented, and a break occurs between the two sorts of markings, due to the failure of the centripetal patch to spread so as to unite with the centrifugal area. In Fig. 19 the sacral patches have wholly failed to develop but the centrifugal patch still covers the distal half of the tail. Possibly the dark heel marks in Fig. 16 are patches developed in the same way. In the house cat, a dark or "smutty" nose is often present in contrast to an otherwise white face, or with the ear patches only slightly reduced. In the breed of rabbits known as "Himalayan," the centrifugal pigmentation remains, though the centripetal markings have disappeared, so that it is pure white except for the black nose, ear tips and toes. No doubt, however, it would be possible for the two types of pigmentation to appear in a single individual. This is suggestive of the winter phase of the Arctic hares, in which the black ear tips contrast strongly with the otherwise white pelage. The physiology of the process whereby certain animals acquire a white winter coat is not yet fully worked out. It is curious that in occasional *melanistic* individuals of the eastern varying hare, the black color is retained throughout the winter, instead of being replaced by white—again a persistence of *black* pigment. In dappled gray horses a black patch sometimes appears on the bridge of the muzzle, usually the first place to show white in the restriction of centipetal pigmentation. The feet may also be black. Among certain antelopes a black muzzle mark is similarly present, and in Hunter's antelope (*Damaliscus hunteri*) a white border partly surrounds such a mark. This, I believe, is due to a slight restriction of the ear patches, sufficient to prevent them from reaching the muzzle, and of about the same nature as seen in the blesbok (*Damaliscus albifrons*) in which, through the *absence* of a centrifugal nose patch, the entire

front of the muzzle is white. The white chevron on the muzzle of several antelope (*Strepsiceros, Taurotragus*) is probably the result of a similar restriction of ear patches combined with a centrifugal nose patch, leaving a white line between. The black dorsal stripe seen in many mammals and the black tail tip are probably manifestations of centrifugal pigmentation. The latter mark is common in stoats (*Mustela*) and among those that change to a white coat in winter, as the ermine, the tail tip still remains black. In sundry other genera, as *Genetta,* a black tail tip is part of the normal pattern.

In their paper on albinistic negroes, Simpson and Castle (1913) published some highly interesting photographs of "piebald" individuals. In four persons of one negro family the hair over the median part of the head from the occiput to forehead is pure white, as though due to a restriction of the aural pigment patches. In addition, more or less of the median area of the back, as well as the hands (including much of the forearms) and feet (including the lower part of the ankle) are pigmented. These latter areas may represent centrifugal pigmentation, but it should be noted that this is present in the dermis. Possibly there is a close relation between dermal pigment and that produced in the centrifugal style of pigmentation.

Among birds, the black of the outer tail feathers of the ptarmigan (*Lagopus*) may be comparable. A black area is also sometimes present on the middle of the throat, or as in certain gulls the outer primaries may be black.

This form of pigmentation is not found universally and the conditions governing its appearance are unknown, though its heredity in the "Himalayan" rabbit has been somewhat studied by Professor Castle.

SUMMARY

The principal points of this paper may be summed up as follows:

1. In mammals and birds that normally are com-

pletely pigmented, there are certain definite points of the body from which as centers the tendency to develop pigment in the epidermal structures may become less and less. Outward from each of these centers pigment formation spreads to include very definite areas which in wholly pigmented animals overlap slightly at their borders or are at least contiguous.

2. A reduction in the area covered by any of these primary patches results in a white mark at the line of junction of two contiguous color patches, where no pigment is produced. These white marks between the primary patches are spoken of as primary breaks.

3. Through a study of the breaks in pied individuals of domesticated species of mammals and birds, the boundaries of the primary patches have been determined. These are homologous in the two groups and subject to a certain amount of variation in different types. They are: a median crown patch unpaired, and five paired patches on the opposite sides of the body, which are named from the general areas they cover, the ear, neck, shoulder, side and rump patches. Their limits are more precisely defined under the different species treated.

4. These patches are physiologically independent of each other and may be differently colored in the same individual.

5. Pied patterns among many wild species have been brought about through the areal reduction of these pigment patches in a definite way so that the white markings resulting as breaks between the reduced patches have become fixed and form a permanent part of the normal pattern.

6. In several wild species this development of white markings is shown to be even now taking place, but the amount of pigment reduction is still fluctuating so that the white markings vary much in extent with different individuals.

7. The development of such white markings takes place probably by little and little, so that the departure from

type is not so great as to arouse antagonism against the varying individual on the part of others of its species. Also, the gradualness of the change allows the species to become accommodated to any disadvantage that might concomitantly arise.

8. The converse of this centripetal style of pigmentation is present in many species, and results in pigmentation (commonly black) at the extremities or along lines where primary breaks occur in the centripetal form, namely at the tip of the nose, ears, tip of the tail or the toes; possibly the black dorsal stripe is due also to centrifugal pigmentation. Patterns may develop as in certain antelopes by a white break between patches of the two types.

In conclusion, I wish to express my indebtedness to Professor W. E. Castle for much helpful criticism and advice, and to the Museum of Comparative Zoology for permission to make record of specimens in its study collection.

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SHORTER ARTICLES AND CORRESPONDENCE

THE BEARING OF THE SELECTION EXPERIMENTS OF CASTLE AND PHILLIPS ON THE VARIABILITY OF GENES

CASTLE and Phillips have recently reviewed the results of six years' work in which they selected for and against "hoodedness" in rats.[1] In "hooded" or "piebald" rats only part of the coat is pigmented; the area of dark (versus white) coat varies greatly in different animals, but tends, in those of medium grade, to cover the head, shoulders and middle of the back, like a hood. Starting with a strain which was probably hybrid, although of unknown ancestry, and selecting during thirteen generations for a larger extent of colored coat ("plus" selection), they succeeded in obtaining animals with a greater and greater area of pigmentation. The average, the mode, and the extremes were raised. Conversely, selection for less pigmentation ("minus" selection) was accompanied by a gradual but decided and continual dimunition in the dark area. "Return" selection also succeeded; that is, plus selection was effective even in a line which was already lighter than the average on account of a previous minus selection, and, *vice versa*, minus selection caused a lightening of a strain that had been made exceptionally dark by a prior plus selection.

Certain crosses proved that more than one factor affecting hoodedness is involved in the difference between the different races. Therefore the production of animals of desired grade by selection may perhaps be explained as a mere sorting out, into different lines of descent, of different combinations of the various factors for hoodedness originally present in the heterozygous ancestors. It is the opinion of Castle and Phillips, however, that this explanation will not suffice to account fully for the continued efficacy of selection in their experiments, and they believe it probable that a factor or factors for hoodedness are undergoing variation of a fluctuating nature.

[1] Castle and Phillips, "Piebald Rats and Selection, An experimental test of the effectiveness of selection and of the theory of gametic purity in Mendelian crosses." Published by the Carnegie Institution of Washington. See also Castle's "Pure Lines and Selection" in *American Breeders' Magazine*, 1914.

A conclusion so radical and so opposed to previous work should not be accepted, however, as long as it remains at all reasonably possible to use instead an explanation in harmony with the results of Johannsen and other investigators. Johannsen dealt with a character—dimensions of seed—which must beyond any doubt have been partially dependent upon a very great many factors, yet he found that selection had no effect whatever after he had separated the different genotypes from one another. Thus he proved the constancy of a great many genes "at one blow"—namely, of all the genes appreciably concerned in seed size. Of course, if there had been a chance for cross-fertilization in his experiments, he, like Castle, would have obtained a result from selection, but this would have been due to recombination, not variation, of genes. All our evidence points to the conclusion that the vast majority of genes are extremely constant, although they differ somewhat in that very slight amount of variation which they do show. For example, in *Drosophila*, although in the case of most genes not more than one mutation has been found, yet in one case (possibly in two or three cases) a locus has mutated three times, each time in a different way, thus giving rise to a system of multiple allelomorphs containing four members. This gene evidently is more subject to mutation than the others, yet this formation of a series of multiple allelomorphs can not even remotely be compared to fluctuating variability, for the three mutations were all large steps (much smaller could easily have been detected), and they were found only during the examination of some millions of individuals in the rest of which the locus was not observed to mutate at all. Some few genes are known, however, which really do change frequently (*e. g.*, that for "variegated" corn), but these cases are extremely rare; moreover, here the degree and nature of the change are fixed, and also, after the change has once occurred the instability of the gene is lost. Thus, in no known case do the variations of a gene among, let us say, several thousand immediate descendants of the individual possessing it, form a probability curve, as neo-Darwinians might perhaps suppose, nor even are any cases known where genes can undergo frequent changes that may vary at all in kind or amount or occur successively.

Let us then inquire into the probability and adequacy of that explanation of Castle and Phillips's results which does not require the assumption that a gene or genes involved change compara-

tively frequently and successively, but which assumes a sorting out of numerous factors. It is now pretty generally accepted by Mendelians that the germ plasm of any of the higher organisms contains a large number of genes, which play various rôles in the numberless processes and reactions of development whereby the egg is transformed into the adult individual. The exact nature and intensity of any one characteristic of this adult organism (*e. g.*, hoodedness in rats) is dependent upon the nature of each of the various reactions which were involved in producing this character, and thus dependent upon all the genes (and environmental factors also) involved in any of those reactions. Now, in an ordinary Mendelian cross, all the individuals are usually homozygous and alike in respect to all but one of the pairs of genes that noticeably affect the character concerned. In such a case, then (so far as differences in environmental influences do not obscure the outcome), one obtains the simple Mendelian results derived from the segregation, at reduction, and recombination, at fertilization, of but this one pair of allelomorphs.

The strain of hooded rats, however, was probably a hybrid between two races of rather remote relationship. When two such races are crossed, the individuals often differ in more than one pair of those factors that affect the character studied, especially if the character is such as to be influenced by a relatively large number of genes. It can not be questioned that some characters are thus determined or influenced by a much larger number of developmental reactions than are others, and such characters will therefore vary more in inheritance, since if a difference exists between two individuals in respect to any given gene, these characters are more likely to be affected than others. Gross size, for example, is a character dependent in this way upon an exceptionally large number of genes, for any gene which influences the size of any organ must affect to some extent the total size. In some other cases in which characters are found to be influenced by relatively many genes, the reason for this is not so evident, *e. g.*, in the case of the red flower-color of flax, or the truncated condition of the wing in some races of *Drosophila*. Here the production of the character may be conceived to be dependent upon some reaction that can be easily modified by various means.[2] For our present purpose we must assume that

[2] It is conceivable that differences in respect to numerous genes have sometimes arisen even in the case of characters not naturally very easily

the character "hoodedness" belongs in this class and that the ancestral hooded rats used by Castle and Phillips were the descendants of a cross involving many genes for that character.

The results of such a cross are of course complicated, for the different pairs of allelomorphs generally can undergo recombination at the reduction division of the hybrid, so that in F_2 or subsequent generations as many different genetic types of individuals are formed as there are possible different combinations of those factors wherein the ancestors differed. Not all these genetic types, of course, will fall into different phenotypes, yet generally there will be a large number of overlapping phenotypes among the progeny.

The larger the number of factors in which the two ancestral lines differed, the larger will be the number of different possible combinations of these factors, and accordingly the smaller will be the chance of any individual having one of those particular combinations necessary to a relatively high or a relatively low intensity of the character. In other words, the larger the number of factors (for one character) for which a population is heterogeneous, the more numerous are the possible different grades of intensity of this character among the different individuals, but the fewer will be the individuals which approach the more extreme grades theoretically possible in such a population.[3] Suppose, for example, that two parents differ in five pairs of factors for hoodedness, which are partially dominant[4] to their allelomorphs and summative in their action. Then in F_2 not one

influenced by diverse means, merely because one of the two races had been subjected to a very long and drastic selection, so that any of those rare mutations which affected that character in the desired direction had in this race been preserved. Selection in such a case, however, would have to involve many millions of individuals.

[3] One extreme, *e. g.*, the "plus," will be rather frequent, however, if all the "plus" factors dominate completely. But in the case of the hooded rats we must assume either that dominance is generally incomplete or that in the case of some factors the "minus" allelomorph dominates in the case of others the "plus," since F_1 rats from a cross of the plus by the minus strain are on the average intermediate in type between these two extremes.

[4] It is of course by no means necessary to assume incomplete dominance of the factors. If dominance is complete (in some cases the "minus" factor may dominate, in others the "plus"), the rigor of selection will be diminished, since heterozygous forms can not be distinguished from homozygous. Therefore, although a somewhat greater number of individuals will be found having the limiting values, it will take longer to bring the average up to the limit.

individual in a thousand will have the most extreme dark or light grade of hoodedness possible. However, by selecting the more extreme individuals, and mating them together, a still more extreme grade of hoodedness may be obtained in F_3 (both as to average and limiting values), and the same process may be continued for a good many generations. The number of generations during which effective selection is possible depends on the number of factors concerned, the rigor of selection, and the amount of inbreeding of brother to sister.

In regard to the latter point, since brother and sister are much more apt to be alike in their genetic constitution than are other individuals, offspring from such a mating are more apt to be homozygous and alike, or, we may say, such offspring will tend to be homozygous and alike in a larger number of factors; then, mating two individuals homozygous for these factors together, there will be much less variation and so less opportunity to continue selection among their progeny. In the case of Castle and Phillips's experiments, however, no such attempt at inbreeding was reported. Here, then, the individuals mated together would be more apt to differ genetically, even though they looked alike (thus, one might be AA bb, the other aA bB), and their descendants would therefore present a larger number of different combinations of factors for the selector. Often a greater effect may be eventually produced in this manner than by inbreeding, for a larger number of combinations of factors are thus produced, some of which may be of more extreme type. The effect would usually be slower, however, since such matings tend to keep the strain heterozygous and are often steps backwards. Cross-breeding, then, will help to explain the relatively slow but long-continued and eventually large effect of selection in Castle and Phillips's experiments, although such a result could also be obtained without cross-breeding if the factors were numerous enough.

The "return selections" also are easily explicable on the multiple factor view. Due to the original difference in so many factors, and the fact that cross-breeding diminishes the tendency to homozygosis which selection favors, the rats were presumably heterozygous even after generations of selection. They would not be as heterozygous as before, of course, and, correspondingly, Castle and Phillips did find less variation in the rats after selection. Yet there would still be a good chance for recombination,

and an alteration in the race could therefore be produced by further selection or by return selection. As we have seen, this is especially true if certain factors are completely dominant, although dominance is by no means a necessary condition.

As a very simple illustration, let us suppose that the "plus" factors A and B dominate over the "minus" factors "a" and "b," respectively, and each increase the pigmented area to about the same extent. To begin with, two moderately hooded individuals, Aa bb and aa Bb, were mated together. They produced 1aa bb—light-hooded, 1aa Bb and 1Aa bb—both moderate, and 1Aa Bb—dark. We first select for dark; mating the dark rats together, 9 darks, 6 moderates, and 1 light, would be produced (F_2). The average color of the offspring has thus been increased by selection (the limiting color, too, if dominance is incomplete). It can be still further increased in subsequent generations. On the other hand, the color can be made lighter again by a "return selection," for if, instead of mating the F_2 or F_3 darks together, we mate the moderates or mate darks with moderates, many of the matings will give offspring lighter, on the average, than in the preceding generation; *e. g.*, Aa Bb by Aa bb gives 3 dark, 4 moderate, 1 light, as compared with the previous 9 dark, 6 moderate, 1 light. In subsequent generations, the average could be brought still lower.

Let us now see whether there is any experimental evidence in support of the multiple factor explanation of Castle and Phillips's results, aside from the fact that it is adequate and is the only one consistent with other work. One point of evidence we have noted—the variability of the rats continued to decrease as a result of selection in either direction. This we should of course expect on the multiple factor view, for selection gradually tends towards homogeneity in a population, even though it may require a long time to produce complete homogeneity. The second and strongest evidence is from crosses.

The crosses show that one of the factors concerned in differentiating hooded rats from wild rats, which are pigmented all over, or from "Irish" rats, which are almost completely pigmented, is "hypostatic." In other words, a rat having the normal allelomorphs of this factor will always be self-colored, or nearly so; one having the other allelomorphs will always be distinctly hooded, although the amount of the hoodedness varies. "Self," as it happens, is dominant, in this case, over hooded.

Thus, on crossing a hooded to a wild or Irish rat, all the F_1 are self (or nearly so); in F_2 there are three selfs to one hooded, but the hoodeds vary in intensity. The question then is, does this variation (so far as it is not due to "environmental" differences) depend upon what other "epistatic" or "modifying" factors for hoodedness may or may not be present, or is there evidence that it depends instead, or in addition, upon a variability of one or more of the factors for hoodedness? As will be shown below, it can be proved that different combinations of modifying factors do occur in the different hooded indiviuals: this being true, there can be no ground for making the unusual postulate that in this case or in the selection experiments a factor or factors concerned undergo variation.

The proof is that when light hooded rats from the minus strain are crossed to wild or Irish rats the hooded rats in F_2 vary much more than did the original strain of hooded rats and average much darker. Obviously, the P_1 hooded rats differed from the wild or Irish in a number of modifiers as well as in the hypostatic factor; moreover, as we should have expected, this difference consisted chiefly in the fact that the wild or Irish rats contained "plus" allelomorphs in place of some of the "minus" modifiers present in the P_1 strain that had undergone minus selection. Thus the F_2 hooded rats, containing various combinations of these modifying factors wherein the two strains differed, varied much more than did the parental strain of hooded rats, and were on the average much darker.

In order to escape this conclusion that modifying factors were involved, Castle and Phillips at first postulated that the reason that the F_2 hooded were darker than the original "minus" strain was because the factor for hooded had in many cases become contaminated by its allelomorph (the factor for self) in the F_1 rats. This is violating one of the most fundamental principles of genetics—the non-mixing of factors—in order to support a violation of another fundamental principle—the constancy of factors. The refutation of their supposition came unexpectedly soon. It would be expected, on the view of multiple factors, that the wild or Irish rats (containing the allelomorph for self in place of the hypostatic factor for hooded) would not possess as many "minus" modifiers as the hooded strain which had been specially selected to contain as many of these as possible; neither would these "self" rats contain as many "plus" modifiers as the

hooded strain which had undergone plus selection (and which so contained nearly all of the plus modifiers originally present in *either* the self or the hooded ancestors). Thus it was to be expected that, just as a cross of self with the minus race gave F_2 hooded rats darker than the original minus strain, so a cross of wild or Irish rats with hoodeds resulting from the plus selection would give F_2 hooded rats *lighter* than those of the plus strain. This result was actually obtained. It was fatal to the idea that the difference between the P_1 strain of hooded rats and the F_2 hoodeds was due to contamination of the allelomorph for hooded with that for self, since such contamination should have resulted in F_2 hooded rats *darker* than those of P_1, not lighter. For wild and Irish rats are both much more extensively pigmented than hoodeds even of the plus strain.

The change in hoodedness from P_1 to F_2 was therefore due to recombinations of the modifying factors wherein the two strains differed. That many such modifiers were concerned is indicated by the evenly distributed variability of the F_2 hoodeds and the fact that very few were as extreme as the hooded grandparents. The same fact is brought out in a cross of the minus with the plus race; here no clear-cut ratios were obtainable, the classification into different genotypes being rendered impossible by the multiplicity of factors (no one of which was hypostatic as in the other crosses). Of course, this knowledge of so many factors being concerned in the crosses helps our interpretation of the selection results decidedly, for the more numerous are the factors concerned, the longer would it be possible to continue an effective selection on the progeny of the hybrids, and the original hooded rats of the selection experiments were admittedly in all likelihood descended from just such hybrids. The exact number and effect of the different factors can not be determined from Castle and Phillip's data, since to do this very special crosses must be made and individual pedigrees kept. Selection experiments can be of little value so long as there are factors for which the individuals may be heterozygous, unless these factors can be accurately followed in inheritance.

Of course, it is quite possible that in the course of these long-continued experiments mutations affecting the hoodedness occasionally happened to arise, especially since it seems likely that this character is dependent upon an unusually large number of genes; for then, as a matter of mere chance, any mutation which

occurred would be more likely to affect it than it would be to affect most characters. It is interesting to note that one such mutation, of a very marked and unquestionable character, was in fact observed. The mutant factor proved to be a strong "plus" modifier, which was almost completely dominant, and itself showed no contamination or variation, so far as could be determined. It arose, as it happened, in the plus strain. A part of the effectiveness of selection may therefore have been due to the occurrence and sorting out of such occasional mutations, but there is no way of telling how many of these took place, or *any* need for assuming them at all in explaining the result. These rare mutations, however, would form a very different phenomenon from such fluctuating or frequent and progressive variation of a gene or genes concerned as Castle postulates. Although the academic possibility of variation of the latter type can not be denied, there is no experimental evidence which can be used to support it, and there is good evidence against it in many individual cases.

It is difficult to believe that this suggestion of Castle and Phillips was not made in a spirit of mysticism, when we consider also their suggestion that the genes may undergo contamination, and especially when we consider the following passage, with which their paper concludes:

> It seems to us quite improbable that the plus mutation could have arisen in the minus selection series. We believe that the repeated selection which was practised had something to do with inducing this change in the plus direction. If one can increase at will the "modifiers" which make the pigmentation more extensive, it does not seem strange that after a time a readjustment should occur within the cell which should incorporate modifiers in that part of the cell which is responsible for the unit-character behavior of the hooded pattern. This would amount to a quantitative change in the unit-character for hooded pigmentation.

To thus suppose that independent genes *fuse* or induce changes in one another, merely because they happen to produce similar *end effects* upon the organism, and in spite of the fact that they usually lie in different chromosomes and are apt to differ from each other as much as do other genes, is utterly teleological.

A paper by A. L. and A. C. Hagedoorn criticizing Castle's work and conclusions, appeared at the same time as the paper of

Castle and Phillips.[5] The Hagedoorns champion the multiple factor hypothesis as an explanation of Castle's results, and also cite certain rather inconclusive experiments of their own to support this point of view. They err, however, in supposing that the factors concerned must be incompletely dominant; as we have seen, this is not a necessary assumption, if we admit that in the case of some modifiers the "minus" allelomorph dominates, in others the "plus." They also err in denying the possibility, on the multiple factor view, of successful "return selection," if inbreeding be strictly followed. In fact they offer this as a test of their point of view. As we have seen, "return selection" would be possible in some cases, even if the animals were inbred; and in Castle and Phillips's experiments, where inbreeding was not followed, "return selection" was certainly very effective.

Finally, papers have recently appeared by MacDowell,[6] in which he gives evidence that certain other cases of inheritance (*e. g.*, head size in rabbits), formerly considered by Castle to support the idea of genic variation and contamination, are probably best interpreted on the view of multiple factors instead. His evidence consists in the fact that the characters concerned are somewhat more variable in the offspring of back-crosses than in F_1, as we should expect on the basis of recombination of multiple factors, but which he believes could not plausibly be explained otherwise.

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[5] A. L. & A. C. Haagedorn, "Studies on Variation and Selection," *Zeit. f. ind. Abst. u. Verab.*, 1914.

[6] E. C. MacDowell, "Multiple Factors in Mendelian Inheritance," *Jour. Exp. Zool.*, 1914, and Carnegie Inst. of Wash., 1914.